

IN THE CLAIMS

1. (currently amended) A single chain T cell receptor (scTCR) comprising:

an α segment constituted by a human TCR α chain variable region sequence fused to the N terminus of a human TCR α chain constant region extracellular sequence,

a β segment constituted by a human TCR β chain variable region sequence fused to the N terminus of a human TCR β chain constant region extracellular sequence, and

a linker sequence linking the C terminus of the α segment to the N terminus of the β segment, or vice versa,

the constant region extracellular sequences of the α and β segments being linked by a disulfide bond,

the length of the linker sequence and the position of the disulfide bond being such that the variable region sequences of the α and β segments are mutually orientated substantially as in native $\alpha\beta$ T cell receptors, wherein the scTCR is selected from the group consisting of:

(a) an scTCR wherein the constant region extracellular sequence of the α segment includes a sequence corresponding ~~corresponds~~ to TRAC*01 and the β segment includes a sequence corresponding to TRBC1*01 or TRBC2*01, and a ~~the said~~ non-native disulfide bond is between cysteine residues substituted for Thr 48 of exon 1 of TRAC*01 and Ser 57 of exon 1 of TRBC1*01 or TRBC2*01;

- (b) an scTCR wherein a disulfide bond links cysteine residues substituted for Thr 45 of exon 1 of TRAC*01 and Ser 77 of exon 1 of 1 or
TRBC1*01 or TRBC2*01 or TRBC2*01;
- (c) an scTCR wherein a disulfide bond links cysteine residues substituted for Tyr 10 of exon 1 of TRAC*01 and Ser 17 of exon 1 of 1 or
TRBC1*01 or TRBC2*01;
- (d) an scTCR wherein a disulfide bond links cysteine residues substituted for Thr 45 of exon 1 of TRAC*01 and Asp 59 of exon 1 of 1 or
TRBC1*01 or TRBC2*01 or TRBC2*01; and
- (e) an scTCR wherein a disulfide bond links cysteine residues substituted for Ser 15 of exon 1 of TRAC*01 and Glu 15 of exon 1 of 1 or
TRBC1*01 or TRBC2*01 or TRBC2*01.

2-4. (canceled)

5. (currently amended) A scTCR as claimed in claim 1 ~~3~~ wherein the constant region extracellular sequence present in the α segment includes a sequence corresponding to the extracellular constant Ig domain of a TCR α chain, and/or the constant region extracellular sequence present in the β segments includes a sequence corresponding to the extracellular constant Ig domain of a TCR β chain.

6. (previously presented) A scTCR as claimed in claim 1 wherein (a) the α segment is the variable region of a TCR fused to the N terminus of the extracellular domain of the α chain constant region of a TCR α chain; and/or (b) the β segment is the variable region of a TCR β chain fused to the N terminus of the extracellular domain of the constant region of a TCR β chain.

7. (previously presented) A scTCR as claimed in claim 1 wherein the constant region extracellular sequences present in the α and β segments correspond to the constant regions of the α and β chains of a native TCR truncated at their C termini such that the cysteine residues which form the native interchain disulfide bond of the TCR are excluded.

8. (previously presented) A scTCR as claimed in claim 1 wherein the constant region extracellular sequences present in the α and β segments correspond to the constant regions of the α and β chains of a native TCR in which cysteine residues which form the native interchain disulfide bond are substituted by another amino acid residue.

9. (original) A scTCR as claimed in claim 8, wherein the said cysteine residues are substituted by serine or alanine.

10. (previously presented) A scTCR as claimed in claim 1 wherein the linker sequence has the formula -P-AA-P- wherein P is proline and AA represents an amino acid sequence wherein the amino acids are glycine and serine.

11. (previously presented) A scTCR as claimed in claim 1 wherein the linker sequence links the C terminus of the α domain to the N terminus of the β domain.

12. (original) A scTCR as claimed in claim 11 wherein the linker sequence consists of from 26 to 41 amino acids.

13. (original) A scTCR as claimed in claim 11 wherein the linker sequence consists of 29, 30, 31 or 32 amino acids.

14. (original) A scTCR as claimed in claim 11 wherein the linker sequence consists of 33, 34, 35 or 36 amino acids.

15. (previously presented) A scTCR as claimed in claim 11 wherein the linker sequence is- PGGG-(SGGGG)₅-P- (SEQ ID NO:1) wherein P is proline, G is glycine and S is serine.

16. (previously presented) A scTCR as claimed in claim 11 wherein the linker sequence is- PGGG-(SGGGG)₆-P- (SEQ ID NO:34) wherein P is proline, G is glycine and S is serine.

17. (previously presented) A sTCR as claimed in claim 1 in which an unpaired cysteine residue present in native TCR β chain is not present.

18. (currently amended) A scTCR as claimed in claim 1, wherein the constant region extracellular sequence of the α segment includes a sequence corresponding ~~corresponds~~ to TRAC*01 and the β segment includes a sequence corresponding to TRBC1*01 or TRBC2*01, and a ~~the said~~ non-native disulfide bond is between cysteine residues substituted for Thr 48 of exon 1 of TRAC*01 and Ser 57 of exon 1 of TRBC1*01 or TRBC2*01.

19. (withdrawn – currently amended) A scTCR as claimed in claim 1, wherein a disulfide bond links cysteine residues substituted for Thr 45 of exon 1 of TRAC*01 and Ser 77 of exon 1 of TRBC1*01 or TRBC2*01.

20. (withdrawn – currently amended) A scTCR as claimed in claim 1, wherein a disulfide bond links cysteine residues substituted for Tyr 10 of exon 1 of TRAC*01 and Ser 17 of exon 1 of TRBC1*01 or TRBC2*01.

21. (withdrawn – currently amended) A scTCR as claimed in claim 1, wherein a disulfide bond links cysteine residues substituted for Thr 45 of exon 1 of TRAC*01 and Asp 59 of exon 1 of TRBC1*01 or TRBC2*01.

22. (withdrawn – currently amended) A scTCR as claimed in claim 1, wherein a disulfide bond links cysteine residues substituted for Ser 15 of exon 1 of TRAC*01 and Glu 15 of exon 1 of TRBC1*01 or TRBC2*01.

23-25. (canceled)

26. (previously presented) A scTCR as claimed in claim 1 wherein the TCR is one which binds a peptide MHC complex.

27. (canceled)

28. (withdrawn – previously presented) A scTCR as claimed in claim 1 wherein the TCR is one which binds a superantigen or a peptide-MHC/superantigen complex.

29. (withdrawn – previously presented) A multivalent T cell receptor (TCR) complex comprising a plurality of sTCRs as claimed in claim 1.

30. (previously presented) A scTCR as claimed in claim 1 which is covalently linked to a therapeutic agent.

31. (previously presented) A scTCR as claimed in claim 1, or a plurality thereof, when attached to a particle or bead.

32. (previously presented) A composition comprising a scTCR as claimed in claim 1 and a pharmaceutically acceptable carrier.

33. (withdrawn – previously presented) A method for detecting a TCR ligand selected from MHC-peptide complexes, CD 1-antigen complexes, superantigens and MHC-peptide/superantigen complexes which comprises: providing a scTCR as claimed in claim 1, or a plurality thereof; contacting the scTCR with the TCR ligand; and detecting binding of the scTCR to the ligand.

34. (withdrawn – previously presented) A method of identifying an inhibitor of the interaction between an scTCR as claimed in claim 1, or a plurality thereof, and a TCR ligand selected from MHC-peptide complexes, CD 1-antigen complexes, superantigens and MHC-peptide/superantigen complexes comprising contacting the scTCR with a scTCR ligand binding partner, in the presence of and in the absence of a test compound, and determining whether the

presence of the test compound reduces binding of the scTCR to the TCR ligand, such reduction being taken as identifying an inhibitor.

35. (withdrawn – previously presented) A method of identifying a potential inhibitor of the interaction between an scTCR as claimed in claim 1, or a plurality thereof, and a TCR ligand selected from MHC-peptide complexes, CD 1-antigen complexes, superantigens and MHC-peptide/superantigen complexes comprising contacting the scTCR or scTCR ligand binding partner with a test compound and determining whether the test compound binds to the scTCR and/or the TCR ligand, such binding being taken as identifying a potential inhibitor.

36. (withdrawn – previously presented) A nucleic acid molecule comprising a sequence encoding a scTCR as claimed in claim 1, or a sequence complementary thereto.

37. (withdrawn) A vector comprising a nucleic acid molecule as claimed in claim 36.